***Syzygium samarangense* leaf extract exhibits distinct antidiabetic activities: Evidences from *in silico* and *in vivo* studies**

Rasha M.H. Rashied1,\*, Mohamed A.O. Abdelfattah2, Hesham A El-Beshbishy3, Assem M. ElShazly4, Mona F. Mahmoud5, Mansour Sobeh6,\*

1School of Life and Medical Sciences, University of Hertfordshire hosted by Global Academic Foundation, New Administrative Capital, Cairo 11835, Egypt

2College of Engineering and Technology, American University of the Middle East, Kuwait

3Biochemistry Department, Faculty of Pharmacy, Al-Azhar University, Nasr City, Cairo 11751, Egypt

4Department of Pharmacognosy, Faculty of Pharmacy, Zagazig University, Zagazig 44519, Egypt

5Department of Pharmacology and Toxicology, Faculty of Pharmacy, Zagazig University, Zagazig 44519, Egypt

6AgroBioSciences, Mohammed VI Polytechnic University, Lot 660–Hay MoulayRachid, Ben-Guerir 43150, Morocco

Corresponding authors:

Emails: rasha.rashied@gmail.com, mansour.sobeh@um6p.ma

**Table 1S**. Docking scores of 86 phenolic acids identified from *S. samarangense* on PPARɣ and GLP-1. Compounds are arranged according to PPARɣ scores.

|  |  |
| --- | --- |
| **Compounds** | **Docking score (kcal/mol)** |
| **PPARɣ** | **GLP-1** |
| 1-Sinapoyl-2-feruloylgentiobiose | -28.79 | -10.42 |
| 1,2-Disinapoylgentiobiose | -28.02 | -12.63 |
| Valoneic acid dilactone | -24.82 | -11.14 |
| 3,4-Dicaffeoylquinic acid | -22.38 | -11.98 |
| Ellagic acid arabinoside | -21.56 | -10.34 |
| 4,5-Dicaffeoylquinic acid | -21.32 | -10.54 |
| 3,5-Diferuloylquinic acid | -21.05 | -10.45 |
| 3,4-Diferuloylquinic acid | -20.54 | -11.38 |
| Chicoric acid | -20.29 | -11.55 |
| 5-Sinapoylquinic acid | -20.15 | -9.64 |
| Sinapine | -18.79 | -8.06 |
| 5-5'-Dehydrodiferulic acid | -18.55 | -11.16 |
| Galloyl glucose | -18.46 | -11.45 |
| 3,5-Dicaffeoylquinic acid | -18.28 | -10.03 |
| Rosmarinic acid | -17.85 | -10.43 |
| Sitosterol ferulate | -17.74 | -9.30 |
| Ellagic acid glucoside | -17.66 | -9.75 |
| 5-8'-Dehydrodiferulic acid | -17.63 | -9.83 |
| 3-Sinapoylquinic acid | -17.24 | -10.59 |
| 5-Caffeoylquinic acid | -17.05 | -11.25 |
| 4-Sinapoylquinic acid | -16.83 | -11.29 |
| 8-*O*-4'-Dehydrodiferulic acid | -16.38 | -10.70 |
| Gallic acid 4-*O*-glucoside | -16.02 | -10.55 |
| 4-Caffeoylquinic acid | -15.78 | -8.71 |
| 5-*O*-Galloylquinic acid | -15.73 | -8.99 |
| Protocatechuic acid 4-*O*-glucoside | -15.49 | -10.63 |
| Feruloyl tartaric acid | -15.49 | -10.68 |
| 4-Feruloylquinic acid | -15.30 | -10.37 |
| Gallic acid 3-*O*-gallate | -15.24 | -11.36 |
| Isoferulic acid | -15.14 |  N/A |
| Avenanthramide 2p | -15.12 | -9.10 |
| Ellagic acid | -15.07 | -9.28 |
| Caffeoyl tartaric acid | -14.95 | -10.57 |
| 4-Hydroxybenzoic acid 4-*O*-glucoside | -14.86 | -9.72 |
| 5-Feruloylquinic acid | -14.68 | -8.97 |
| 5-*p*-Coumaroylquinic acid | -14.68 | -10.97 |
| *p*-Coumaroyl glucose | -14.61 | -8.69 |
| 5-8'-Benzofuran dehydrodiferulic acid | -14.53 | -12.45 |
| Caffeoyl aspartic acid | -14.34 | -9.45 |
| Trans- *p*-Coumaroyl tyrosine  | -14.28 | -8.05 |
| *p*-Coumaric acid 4-*O*-glucoside | -14.22 | -9.67 |
| Caffeic acid ethyl ester | -14.14 | -7.60 |
| 3-*p*-Coumaroylquinic acid | -14.13 | -11.11 |
| Caffeoyl glucose | -13.89 | -8.46 |
| 24-Methyllathosterol ferulate | -13.87 | -9.18 |
| *p*-Coumaroylquinic acid | -13.58 | -9.71 |
| Feruloyl glucose | -13.57 | -7.35 |
| 2,6-Dihydroxybenzoic acid | -13.51 | -7.90 |
| Avenanthramide 2f | -13.31 | -10.91 |
| Caffeic acid 4-*O*-glucoside | -12.87 | -11.83 |
| Dihydrocaffeic acid | -12.67 | -7.64 |
| *p*-Coumaroyl tartaric acid | -12.63 | -10.16 |
| Cis-*p*-Coumaroyl tyrosine  | -12.62 | -9.97 |
| Hydroxycaffeic acid | -12.55 | -9.02 |
| Avenanthramide 2c | -12.40 | -10.41 |
| 4-*p*-Coumaroylquinic acid | -12.32 | -10.97 |
| Cinnamoyl glucose | -12.26 | -9.80 |
| 2,3-Dihydroxybenzoic acid | -11.96 | -8.62 |
| 3-Feruloylquinic acid | -11.82 | -10.01 |
| *p*-Coumaroyl malic acid | -11.65 | -9.61 |
| *m*-Coumaric acid | -11.32 | -7.24 |
| *p*-Coumaroyl glycolic acid | -11.32 | -8.37 |
| Dihydro-*p*-coumaric acid | -10.62 | -8.74 |
| 3,4-Dihydroxyphenylacetic acid | -10.58 | -8.27 |
| Gallic acid ethyl ester | -10.35 | -7.43 |
| *p*-Coumaric acid ethyl ester | -10.30 | -6.59 |
| 2,4-Dihydroxybenzoic acid | -10.14 | -7.81 |
| Sinapic acid | -10.13 | -8.76 |
| Homovanillic acid | -10.06 | -8.34 |
| Protocatechuic acid | -10.04 | -7.43 |
| Caffeic acid | -9.85 | -7.80 |
| Gallic acid | -9.73 | -8.71 |
| Homoveratric acid | -9.35 | -9.85 |
| *p*-Coumaric acid | -9.16 | -7.31 |
| Vanillic acid | -9.02 | -7.37 |
| 3,5-Dihydroxybenzoic acid | -8.92 | -8.62 |
| 4-Hydroxybenzoic acid | -8.84 | -8.09 |
| *o*-Coumaric acid | -8.80 | -7.18 |
| Gentisic acid | -8.79 | -7.08 |
| Ferulic acid | -8.22 | -8.80 |
| 2-Hydroxybenzoic acid | -8.16 | -7.13 |
| Methoxyphenylacetic acid | -8.13 | -6.70 |
| Benzoic acid | -7.85 | -7.80 |
| Cinnamic acid | -7.72 | -7.61 |
| Syringic acid | -7.71 | -8.23 |
| 4-Hydroxyphenylacetic acid | -7.63 | -9.46 |

**Table 2S**. Docking scores of 139 flavonoids identified from *S. samarangense* on PPARɣ and GLP-1. Compounds are arranged according to PPARɣ scores.

|  |  |
| --- | --- |
| **Compounds**  | **Docking score (kcal/mol)** |
| **PPARɣ** | **GLP-1** |
| Naringin 6'-malonate | -30.90 | -10.69 |
| Rhoifolin 4'-*O*-glucoside | -30.75 | -9.63 |
| Kaempferol 3-*O*-xylosyl-rutinoside | -29.39 | -14.51 |
| Kaempferol 3-*O*-rhamnosyl-rhamnosyl-glucoside | -29.04 | -10.89 |
| Chrysoeriol 7-*O*-(6''-malonyl-apiosyl-glucoside) | -28.94 | -10.90 |
| Isorhamnetin 3-*O*-rutinoside | -28.66 | -11.22 |
| Quercetin 3-*O*-xylosyl-rutinoside | -28.23 | -12.33 |
| Myricetin 3-*O*-rutinoside | -28.14 | -13.16 |
| Quercetin 3-*O*-(6''-acetyl-galactoside) 7-*O*-rhamnoside | -28.04 | -12.22 |
| Neodiosmin | -27.33 | -9.75 |
| Kaempferol 3-*O*-(2''-rhamnosyl-galactoside) 7-*O*-rhamnoside | -27.28 | -12.38 |
| Quercetin 3-*O*-sophoroside | -26.47 | -13.11 |
| Luteolin 7-*O*-rutinoside | -26.44 | -14.35 |
| Naringin 4'-*O*-glucoside | -26.38 | -12.65 |
| Quercetin 3-*O*-galactoside 7-*O*-rhamnoside | -26.20 | -11.22 |
| Neoeriocitrin | -26.11 | -11.28 |
| Luteolin 7-*O*-(2-apiosyl-glucoside) | -26.08 | -11.74 |
| Vitisin A | -26.03 | -11.16 |
| Apigenin 7-*O*-(6''-malonyl-apiosyl-glucoside) | -26.01 | -12.11 |
| Diosmin | -25.97 | -15.80 |
| Neohesperidin | -25.95 | -10.26 |
| Eriocitrin | -25.49 | -9.24 |
| Isorhamnetin 3-*O*-glucoside 7-*O*-rhamnoside | -25.04 | -9.32 |
| Didymin | -24.97 | -10.59 |
| Hesperidin | -24.97 | -14.18 |
| Myricetin 3-*O*-arabinoside | -24.50 | -12.78 |
| Myricetin 3-*O*-galactoside | -24.49 | -10.45 |
| Quercetin 4'-*O*-glucoside | -24.39 | -9.97 |
| Quercetin 7,4'-*O*-diglucoside | -24.16 | -10.37 |
| Chrysoeriol 7-*O*-apiosyl-glucoside | -24.01 | -11.66 |
| Kaempferol 7-*O*-glucoside | -23.70 | -7.60 |
| Kaempferol 3-*O*-galactoside 7-*O*-rhamnoside | -23.69 | -9.04 |
| Kaempferol 3-*O*-(6''-acetyl-galactoside) 7-*O*-rhamnoside | -23.61 | -11.74 |
| Kaempferol 3-*O*-xylosyl-glucoside | -23.59 | -13.71 |
| Isorhoifolin | -23.51 | -10.28 |
| Kaempferol 3-*O*-rutinoside | -23.51 | -10.26 |
| Naringin | -23.47 | -10.91 |
| Poncirin | -23.45 | -10.17 |
| Apigenin 7-*O*-apiosyl-glucoside | -23.23 | -8.94 |
| Quercetin 3-*O*-glucosyl-xyloside | -23.18 | -12.90 |
| Quercetin 3,4'-*O*-diglucoside | -22.94 | -10.43 |
| Apigenin 6,8-di-C-glucoside | -22.85 | -13.00 |
| Myricetin 3-*O*-glucoside | -22.74 | -16.24 |
| Kaempferol 3,7-*O*-diglucoside | -22.61 | -10.61 |
| Kaempferol 3-*O*-sophoroside | -22.51 | -11.99 |
| Kaempferol 3-*O*-acetyl-glucoside | -22.49 | -7.73 |
| Apigenin 6,8-C-arabinoside-C-glucoside | -22.34 | -14.49 |
| Isorhamnetin 7-*O*-rhamnoside | -22.01 | -8.73 |
| Quercetin 3-*O*-rutinoside | -21.83 | -13.90 |
| 6''-*O*-Malonylgenistin | -21.81 | -10.00 |
| Apigenin 6-C-glucoside | -21.41 | -10.15 |
| 6''-*O*-Malonyldaidzin | -21.41 | -10.38 |
| Eriodictyol 7-*O*-glucoside | -21.22 | -9.95 |
| Luteolin 7-*O*-glucoside | -21.17 | -12.82 |
| Luteolin 6-C-glucoside | -21.11 | -8.60 |
| Apigenin 6,8-C-galactoside-C-arabinoside | -20.83 | -11.81 |
| Kaempferol 3-*O*-glucoside | -20.71 | -11.95 |
| Narirutin | -20.69 | -14.36 |
| Chrysoeriol 7-*O*-(6''-malonyl-glucoside) | -20.63 | -11.13 |
| 6,8-Dihydroxykaempferol | -20.47 | -8.36 |
| Quercetin 3-*O*-rhamnoside | -20.38 | -11.41 |
| 6-Hydroxyluteolin 7-*O*-rhamnoside | -20.37 | -9.03 |
| Rhoifolin | -24.99 | -10.17 |
| Mearnsitrin | -20.30 | -13.41 |
| Dihydromyricetin 3-*O*-rhamnoside | -20.25 | -11.25 |
| 6''-*O*-Malonylglycitin | -20.22 | -11.37 |
| 3,5-di-*O*-methyl gossypetin  | -20.19 | -9.28 |
| Genistin | -20.03 | -9.71 |
| Luteolin 7-*O*-malonyl-glucoside | -19.92 | -9.45 |
| Quercetin 3-*O*-glucoside | -19.88 | -11.01 |
| Quercetin 3-*O*-xyloside | -19.69 | -10.91 |
| 6''-*O*-Acetylgenistin | -19.64 | -8.96 |
| Quercetin 3-*O*-galactoside | -19.57 | -12.10 |
| Chrysoeriol 7-*O*-glucoside | -19.51 | -9.14 |
| Kaempferol 3-*O*-galactoside | -18.09 | -11.38 |
| 6''-*O*-Acetyldaidzin | -18.06 | -9.19 |
| 6-Hydroxyluteolin | -18.05 | -7.88 |
| Myricetrin | -17.95 | -10.43 |
| Apigenin 7-*O*-glucoside | -17.89 | -9.57 |
| Isorhamnetin 3-*O*-glucoside | -17.88 | -11.08 |
| Baicalein | -17.53 | -7.68 |
| Daidzin | -17.48 | -8.49 |
| Naringenin 7-*O*-glucoside | -17.44 | -7.89 |
| 6''-*O*-Acetylglycitin | -17.20 | -8.61 |
| Quercetin 3-*O*-acetyl-rhamnoside | -17.06 | -12.03 |
| 6-Geranylnaringenin | -17.05 | -10.33 |
| Quercetin 3-*O*-arabinoside | -17.00 | -11.58 |
| Glycitin | -16.82 | -9.52 |
| 7,3',4'-Trihydroxyflavone | -16.81 | -7.67 |
| Cirsilineol | -16.61 | -9.12 |
| Myricetin | -16.39 | -8.43 |
| Dihydroquercetin | -16.21 | -8.48 |
| Quercetin | -16.15 | -9.36 |
| Kaempferol 3-*O*-rhamnoside | -16.03 | -12.72 |
| Nepetin | -16.03 | -8.88 |
| Hispidulin | -15.90 | -7.72 |
| Morin | -15.85 | -9.60 |
| Methylgalangin | -15.61 | -8.83 |
| Rhamnetin | -15.57 | -8.32 |
| Sakuranetin | -15.56 | -8.61 |
| Nobiletin | -15.51 | -10.38 |
| Scutellarein | -15.35 | -8.48 |
| Isorhamnetin | -17.33 | -8.80 |
| Kaempferol | -16.22 | -7.85 |
| Tangeretin | -15.14 | -10.13 |
| 8-Prenylnaringenin | -15.11 | -9.93 |
| Sinensetin | -15.10 | -10.18 |
| Eupatorin | -15.02 | -7.84 |
| Kaempferide | -14.86 | -8.55 |
| Luteolin | -14.81 | -8.13 |
| Pebrellin | -14.74 | -10.21 |
| Eriodictyol | -14.63 | -7.79 |
| 3,7-Dimethylquercetin | -14.47 | -10.19 |
| Demethoxymatteucinol | -14.40 | -8.64 |
| 5,7-dihydroxy-6,8-dimethylflavanone | -14.30 | -9.16 |
| Galangin | -14.22 | -8.41 |
| Genistein | -14.11 | -8.72 |
| Gardenin B | -14.00 | -10.11 |
| Geraldone | -13.96 | -8.23 |
| 3-Methoxysinensetin | -13.85 | -9.88 |
| Biochanin A | -13.81 | -8.85 |
| 3-Methoxynobiletin | -13.76 | -11.81 |
| Hesperetin | -13.69 | -9.32 |
| Glycitein | -13.61 | -8.67 |
| Jaceosidin | -13.45 | -8.14 |
| Cirsimaritin | -13.33 | -8.08 |
| Cryptostrobin | -13.24 | -7.07 |
| (S)-pinocembrin | -13.24 | -7.35 |
| Pinocembrin | -13.23 | -9.55 |
| 8-methylpinocembrin | -13.23 | -7.53 |
| Naringenin | -15.72 | -7.80 |
| Apigenin | -13.17 | -7.65 |
| Chrysin | -12.99 | -7.44 |
| Tetramethylscutellarein | -11.78 | -9.36 |
| 7-Hydroxy-5-methoxy-6,8-dimethylflavanone | -11.76 | -8.64 |
| 7,4'-Dihydroxyflavone | -11.73 | -7.32 |
| 6-Prenylnaringenin | -11.29 | -8.48 |
| Daidzein | -9.76 | -8.07 |
| Formononetin | -9.59 | -8.12 |

**Table 3S**. Docking scores of 29 lignans identified from *S. samarangense* on PPARɣ and GLP-1. Compounds are arranged according to PPARɣ scores.

|  |  |
| --- | --- |
| **Compounds**  | **Docking score (kcal/mol)** |
| **PPARɣ** | **GLP-1** |
| Lariciresinol | -18.71 | -8.81 |
| Medioresinol | -17.52 | -10.38 |
| Episesamin | -17.35 | -7.78 |
| Nortrachelogenin | -17.07 | -10.57 |
| Conidendrin | -16.57 | -11.22 |
| Sesaminol | -16.44 | -7.64 |
| 7-Hydroxysecoisolariciresinol | -16.38 | -10.20 |
| Matairesinol | -16.35 | -8.48 |
| Sesamin | -16.31 | -9.05 |
| Sesamolinol | -15.91 | -8.62 |
| Cyclolariciresinol | -15.90 | -8.96 |
| Trachelogenin | -15.36 | -12.26 |
| Episesaminol | -15.24 | -9.06 |
| Todolactol A | -15.24 | -12.12 |
| Pinoresinol | -15.15 | -9.07 |
| Secoisolariciresinol-sesquilignan | -15.10 | -9.30 |
| Isolariciresinol | -15.06 | -12.62 |
| Sesamolin | -15.06 | -8.32 |
| Syringaresinol | -14.90 | -9.30 |
| 1-Acetoxypinoresinol | -14.89 | -9.12 |
| Lariciresinol-sesquilignan | -14.76 | -8.73 |
| Secoisolariciresinol | -14.67 | -9.81 |
| Anhydro-secoisolariciresinol | -14.38 | -11.74 |
| Arctigenin | -14.34 | -9.35 |
| Isohydroxymatairesinol | -14.31 | -10.35 |
| 7-Hydroxymatairesinol | -13.89 | -9.09 |
| 7-Oxomatairesinol | -13.75 | -8.34 |
| Dimethylmatairesinol | -13.60 | -12.30 |
| Sesamol | -11.13 | -7.31 |

**Table 4S**. Docking scores of 29 tannins identified from *S. samarangense* on PPARɣ and GLP-1. Compounds are arranged according to PPARɣ scores.

|  |  |
| --- | --- |
| **Compounds**  | **Docking score (kcal/mol)** |
| **PPARɣ** | **GLP-1** |
| Theaflavin 3’-*O*-gallate | -31.77 | -13.13 |
| Procyanidin C1 | -31.27 | -15.15 |
| Theaflavin 3-*O*-gallate | -30.16 | -14.16 |
| Prodelphinidin dimer B3 | -30.14 | -14.40 |
| Epiafzelechin-(4b->8)-epicatechin 3,3’-digallate | -28.89 | -13.87 |
| Procyanidin dimer B2 3’-gallate | -28.10 | -11.83 |
| Procyanidin C2 | -27.01 | -8.94 |
| Procyanidin dimer B5 | -26.94 | -10.19 |
| (-)-Epigallocatechin 3-*O*-gallate | -26.60 | -10.91 |
| Procyanidin A1 | -26.58 | -12.05 |
| TellimagrandinII | -25.89 | -9.41 |
| (Epi)-gallocatechin-(epi)-gallocatechin | -25.83 | -12.42 |
| Theaflavin  | -27.77 | -14.50 |
| (-)-Epicatechin gallate | -25.30 | -10.26 |
| Castalagin | -25.27 | -14.05 |
| Procyanidin dimer B7 | -25.09 | -9.80 |
| Procyanidin dimer B1 | -24.89 | -12.36 |
| (-)-Epigallocatechin 3,5-digallate | -24.80 | -11.85 |
| Casuarinin | -24.22 | -11.98 |
| Procyanidin dimer B3 | -24.18 | -9.36 |
| Procyanidin dimer B2 | -23.46 | -12.08 |
| Procyanidin dimer B4 | -22.40 | -12.78 |
| (+)-Catechin 3-*O*-gallate | -21.60 | -8.70 |
| (-)-Epicatechin-(2a-7)(4a-8)-epicatechin 3-*O*-galactoside | -21.44 | -12.51 |
| Catechin 3’-glucoside | -18.81 | -13.26 |
| (+)-Gallocatechin | -16.04 | -9.05 |
| (-)-Epigallocatechin | -14.26 | -9.61 |
| (+)-Catechin | -13.82 | -8.83 |
| (-)-Epicatechin | -10.91 | -9.08 |

**Table 5S**. Docking scores of 61 anthocyanins identified from *S. samarangense* on PPARɣ and GLP-1. Compounds are arranged according to PPARɣ scores.

|  |  |
| --- | --- |
| **Compounds**  | **Docking score (kcal/mol)** |
| **PPARɣ** | **GLP-1** |
| Petunidin 3,5-*O*-diglucoside | -30.61 | -9.99 |
| Petunidin 3-*O*-glucoside | -30.30 | -11.81 |
| Pinotin A | -27.86 | -14.67 |
| Petunidin 3-*O*-galactoside | -27.74 | -11.17 |
| Cyanidin 3-*O*-sophoroside | -27.71 | -13.46 |
| Cyanidin 3-*O*-(6''-succinyl-glucoside) | -27.40 | -12.29 |
| Pelargonidin 3-*O*-glucosyl-rutinoside | -27.38 | -13.03 |
| Pelargonidin 3-*O*-sophoroside | -27.10 | -10.23 |
| Petunidin 3-*O*-(6''-p-coumaroyl-glucoside) | -26.95 | -11.97 |
| Delphinidin 3-*O*-feruloyl-glucoside | -26.89 | -11.70 |
| Delphinidin 3-*O*-rutinoside | -25.94 | -12.69 |
| Cyanidin 3-*O*-glucosyl-rutinoside | -25.74 | -13.23 |
| Cyanidin 3-*O*-(6''-caffeoyl-glucoside) | -25.55 | -11.16 |
| Delphinidin 3-*O*-(6''-p-coumaroyl-glucoside) | -25.31 | -11.48 |
| Malvidin 3-*O*-(6''-acetyl-glucoside) | -25.08 | -10.15 |
| Cyanidin 3-*O*-(6''-p-coumaroyl-glucoside) | -24.89 | -11.85 |
| Petunidin 3-*O*-(6''-acetyl-galactoside) | -24.77 | -11.37 |
| Cyanidin 3-*O*-rutinoside | -24.46 | -12.67 |
| Cyanidin 3-*O*-sambubioside | -24.30 | -12.72 |
| Pelargonidin 3-*O*-sambubioside | -24.25 | -13.55 |
| Petunidin 3-*O*-rutinoside | -24.09 | -11.6 |
| Malvidin 3-*O*-glucoside | -24.06 | -12.71 |
| Malvidin 3,5-*O*-diglucoside | -23.81 | -15.73 |
| Delphinidin 3-*O*-sambubioside | -23.79 | -12.07 |
| Delphinidin 3-*O*-glucosyl-glucoside | -23.71 | -12.1 |
| Peonidin 3-*O*-(6''-p-coumaroyl-glucoside) | -23.41 | -12.26 |
| Cyanidin 3-*O*-(6''-dioxalyl-glucoside) | -23.33 | -12.22 |
| Petunidin 3-*O*-arabinoside | -23.24 | -10.69 |
| Peonidin 3-*O*-glucoside | -23.14 | -12.37 |
| Pelargonidin 3-*O*-rutinoside | -22.98 | -11.09 |
| Cyanidin 3-*O*-(6''-malonyl-glucoside) | -22.77 | -11.21 |
| Delphinidin 3-*O*-(6''-acetyl-glucoside) | -22.69 | -12.18 |
| Pelargonidin 3-*O*-(6''-malonyl-glucoside) | -22.09 | -10.92 |
| Malvidin 3-*O*-galactoside | -21.80 | -13.08 |
| Peonidin 3-*O*-rutinoside | -21.66 | -13.31 |
| Cyanidin 3,5-*O*-diglucoside | -21.58 | -12.57 |
| Delphinidin 3,5-*O*-diglucoside | -21.34 | -12.85 |
| Delphinidin 3-*O*-glucoside | -21.03 | -11.09 |
| Cyanidin 3-*O*-(6''-acetyl-glucoside) | -20.62 | -10.06 |
| Petunidin 3-*O*-(6''-acetyl-glucoside) | -20.45 | -11.09 |
| Pelargonidin 3,5-*O*-diglucoside | -20.16 | -11.43 |
| Delphinidin 3-*O*-galactoside | -20.08 | -11.92 |
| Cyanidin 3-*O*-glucoside | -20.07 | -12.45 |
| Peonidin 3-*O*-(6''-acetyl-glucoside) | -19.96 | -10.92 |
| Peonidin 3-*O*-arabinoside | -19.95 | -12.50 |
| Malvidin 3-*O*-arabinoside | -19.89 | -12.68 |
| Peonidin 3-*O*-(6''-acetyl-galactoside) | -19.74 | -12.54 |
| Pelargonidin 3-*O*-glucoside | -19.58 | -13.26 |
| Peonidin 3-*O*-galactoside | -19.46 | -12.95 |
| Pelargonidin 3-*O*-(6''-succinyl-glucoside) | -19.41 | -11.43 |
| Petunidin 3-*O*-rhamnoside | -19.33 | -11.45 |
| Cyanidin 3-*O*-xyloside | -19.28 | -14.32 |
| Delphinidin 3-*O*-xyloside | -18.42 | -12.21 |
| Cyanidin | -18.37 | -7.76 |
| Cyanidin 3-*O*-(6''-acetyl-galactoside) | -18.14 | -11.39 |
| Pelargonidin 3-*O*-arabinoside | -17.61 | -11.58 |
| Delphinidin 3-*O*-arabinoside | -16.94 | -9.75 |
| Pelargonidin | -16.92 | -7.97 |
| Cyanidin 3-*O*-galactoside | -16.91 | -14.61 |
| Cyanidin 3-*O*-arabinoside | -16.35 | -12.37 |
| Peonidin | -12.46 | -8.53 |

**Table 6S**. Docking scores of 15 chalcones identified from *S. samarangense* on PPARɣ and GLP-1. Compounds are arranged according to PPARɣ scores.

|  |  |
| --- | --- |
| **Compounds** | **Docking score (kcal/mol)** |
| **PPARɣ** | **GLP-1** |
| 3-Hydroxyphloretin 2'-*O*-xylosyl-glucoside | -25.44 | -9.93 |
| Phloretin 2'-*O*-xylosyl-glucoside | -22.65 | -7.52 |
| Phloridzin | -20.73 | -12.27 |
| 3-Hydroxyphloretin 2'-*O*-glucoside | -20.13 | -10.13 |
| Xanthohumol | -16.55 | -9.34 |
| 2’-hydroxy-4’,6’-dimethoxy-3’-methyldihydrochalcone | -15.50 | -8.11 |
| Isoxanthohumol | -15.34 | -9.49 |
| Butein | -14.70 | -7.63 |
| 2’,4’-dihydroxy-6’-methoxy-3’,5’-dimethyldihydrochalcone | -13.96 | -9.67 |
| Aurentiacin (2’-hydroxy-4’,6’-dimethoxy-3’-methylchalcone)  | -13.46 | -8.94 |
| Myrigalone H | -13.40 | -6.80 |
| Phloretin  | -12.81 | -7.85 |
| 2’,4’-dihydroxy-6’-methoxy-3’,5’-dimethylchalcone | -12.50 | -9.18 |
| Stercurensin (2′,4′-Dihydroxy-3′-methyl-6′-methoxychalcone) | -12.43 | -10.39 |
| Uvangoletin | -11.43 | -9.69 |

**Table 7S**. Docking scores of 9 stilbenes identified from *S. samarangense* on PPARɣ and GLP-1. Compounds are arranged according to PPARɣ scores.

|  |  |
| --- | --- |
| **Compounds**  | **Docking score (kcal/mol)** |
| **PPARɣ** | **GLP-1** |
| e-Viniferin | -23.09 | -9.91 |
| d-Viniferin | -21.75 | -11.61 |
| Reservatrol 3-*O*-glucoside | -19.90 | -9.41 |
| Pallidol | -19.29 | -11.85 |
| Piceatannol 3-*O*-glucoside | -17.93 | -9.80 |
| Piceatannol | -13.14 | -6.89 |
| Pinosylvin | -12.21 | -6.75 |
| Reservatrol | -11.64 | -8.21 |
| Pterostilbene | -9.53 | -8.44 |

**Table 8S**. Docking scores of 17 alkylphenols identified from *S. samarangense* on PPARɣ and GLP-1. Compounds are arranged according to PPARɣ scores.

|  |  |
| --- | --- |
| **Compounds** | **Docking score (kcal/mol)** |
| **PPARɣ** | **GLP-1** |
| 5-Tricosenylresorcinol | -17.53 | -8.77 |
| 5-Nonadecenylresorcinol | -16.30 | -7.91 |
| 5-Pentacosenylresorcinol | -16.17 | -7.00 |
| 5-Heneicosylresorcinol | -14.78 | -8.93 |
| 5-Nonadecylresorcinol | -14.31 | -8.62 |
| 5-Tricosylresorcinol | -14.25 | -8.56 |
| 5-Heneicosenylresorcinol | -14.23 | -7.68 |
| 4-Ethylphenol | -12.76 | -5.28 |
| 5-Heptadecylresorcinol | -12.38 | -6.53 |
| 4-Vinylsyringol | -12.31 | -7.76 |
| 5-Pentadecylresorcinol | -11.39 | -8.25 |
| 4-Vinylguaiacol | -11.36 | -7.58 |
| 4-Ethylguaiacol | -11.35 | -7.53 |
| 3-Methylcatechol | -11.12 | -6.20 |
| 4-Ethylcatechol | -10.03 | -6.50 |
| 4-Vinylphenol | -9.87 | -5.26 |
| 4-Methylcatechol | -9.45 | -6.49 |

**Table 9S**. Docking scores of 13 tyrosols identified from *S. samarangense* on PPARɣ and GLP-1. Compounds are arranged according to PPARɣ scores.

|  |  |
| --- | --- |
| **Compounds** | **Docking score (kcal/mol)** |
| **PPARɣ** | **GLP-1** |
| Oleuropein | -21.41 | -12.00 |
| Demethyloleuropein | -20.81 | -13.81 |
| Ligstroside | -19.49 | -12.21 |
| Rosmanol | -18.36 | -11.00 |
| 3,4-DHPEA-EA | -17.54 | -9.64 |
| Oleoside dimethylester | -17.10 | -12.83 |
| Hydroxytyrosol-4-*O*-glucoside | -16.89 | -9.43 |
| 3,4-DHPEA-EDA | -16.78 | -9.55 |
| Oleuropein-aglycone | -16.30 | -9.18 |
| Ligstroside-aglycone | -16.18 | -9.40 |
| Hydroxytyrosol | -11.93 | -6.90 |
| p-HPEA-EDA | -11.73 | -8.53 |
| Tyrosol | -10.13 | -6.74 |

**Table 10S**. Docking scores of 59 terpenes and miscellaneous compounds identified from *S. samarangense* on PPARɣ and GLP-1. Compounds are arranged according to PPARɣ scores.

|  |  |
| --- | --- |
| **Compounds** | **Docking score (kcal/mol)** |
| **PPARɣ** | **GLP-1** |
| Carnosic acid | -20.07 | -8.39 |
| Jambone E | -18.56 | -9.07 |
| Jamunone B | -18.56 | -10.72 |
| Sysamarin B | -17.86 | -7.36 |
| Sysamarin E | -17.76 | -8.65 |
| [6]-Gingerol | -16.68 | -9.06 |
| Jambone G | -16.64 | -7.88 |
| Rosmadial | -15.56 | -11.11 |
| Sysamarin D | -15.50 | -8.84 |
| Jambone F | -14.98 | -9.87 |
| Epirosmanol | -14.79 | -9.58 |
| Betulinic acid | -14.58 | -9.95 |
| Carnosol | -14.15 | -8.54 |
| Phlorin | -13.59 | -12.01 |
| Bisdemethoxycurcumin | -13.53 | -7.83 |
| Esculin | -13.17 | -9.70 |
| Sitosterol | -13.12 | -8.73 |
| Demethoxycurcumin | -13.02 | -9.20 |
| Curcumin | -12.82 | -7.50 |
| Pyrogallol | -12.81 | -6.17 |
| Coumestrol | -12.60 | -7.88 |
| 2,3-Dihydroxy-1-guaiacylpropanone | -12.55 | -7.74 |
| 3,4-Dihydroxyphenylglycol | -12.25 | -8.30 |
| Sysamarin A | -11.97 | -8.66 |
| Cycloartenyl stearate | -11.91 | -8.30 |
| Arbutin | -11.75 | -9.76 |
| Esculetin | -11.68 | -6.77 |
| Betulin | -11.52 | -9.99 |
| Sinapaldehyde | -11.47 | -8.08 |
| Vanillin | -11.39 | -7.69 |
| Mellein | -11.12 | -6.67 |
| Sysamarin C | -10.88 | -9.24 |
| Thymol | -10.80 | -5.94 |
| Ferulaldehyde | -9.94 | -8.05 |
| Isopimpinellin | -9.90 | -7.80 |
| Catechol | -9.90 | -6.53 |
| Juglone | -9.87 | -7.02 |
| 4-Hydroxycoumarin | -9.42 | -6.97 |
| Bergapten | -9.23 | -8.80 |
| Syringaldehyde | -9.02 | -7.66 |
| Protocatechuic aldehyde | -8.91 | -6.48 |
| Xanthotoxin | -8.85 | -6.93 |
| Psoralen | -8.72 | -7.19 |
| Gallic aldehyde | -8.64 | -7.25 |
| Scopoletin | -8.33 | -7.04 |
| Estragole | -8.31 | -6.45 |
| Acetyl eugenol | -8.23 | -6.85 |
| Eugenol | -7.96 | -7.95 |
| Coumarin | -7.95 | -5.69 |
| Carvacrol | -7.90 | -6.15 |
| Guaiacol | -7.68 | -7.49 |
| Umbelliferone | -7.63 | -6.97 |
| 2-Methoxy-5-prop-1-enylphenol | -7.54 | -7.70 |
| 1,4-Naphtoquinone | -7.51 | -6.63 |
| 3-Methoxyacetophenone | -7.35 | -7.53 |
| 4-Hydroxybenzaldehyde | -6.98 | -5.56 |
| p-Anisaldehyde | -6.39 | -6.81 |
| Lupenyl stearate | N/A | -7.79 |
| Squalene | N/A | -8.51 |

**Table 11S**. Docking results of three simulations on PPARɣ receptor for the top 30 compounds.

|  |  |  |
| --- | --- | --- |
| Compound name | PPARɣ docking score (kcal/mol) | Standard deviation |
| **Simulation 1**  | **Simulation 2** | **Simulation 3** |
| **Anthocyanins (9 compounds)** |  |  |  |  |
| Petunidin 3,5-*O*-diglucoside | -30.61 | -30.85 | -30.75 | 0.121 |
| Petunidin 3-*O*-glucoside | -30.30 | -26.47 | -26.48 | 2.208 |
| Pinotin A | -27.86 | -28.01 | -28.01 | 0.087 |
| Petunidin 3-*O*-galactoside | -27.74 | -26.71 | -26.53 | 0.653 |
| Cyanidin 3-*O*-sophoroside | -27.71 | -27.92 | -27.97 | 0.138 |
| Cyanidin 3-*O*-(6''-succinyl-glucoside) | -27.40 | -27.45 | -27.44 | 0.027 |
| Pelargonidin 3-*O*-glucosyl-rutinoside | -27.38 | -27.69 | -27.78 | 0.210 |
| Pelargonidin 3-*O*-sophoroside | -27.10 | -26.02 | -27.16 | 0.642 |
| Petunidin 3-*O*-(6''-p-coumaroyl-glucoside) | -26.95 | -26.74 | -27.14 | 0.200 |
| **Flavonoids (11 compounds)** |  |  |  |  |
| Naringin 6'-malonate | -30.90 | -30.62 | -30.66 | 0.151 |
| Rhoifolin 4'-*O*-glucoside | -30.75 | -30.51 | -30.85 | 0.175 |
| Kaempferol 3-*O*-xylosyl-rutinoside | -29.39 | -29.27 | -29.86 | 0.312 |
| Kaempferol 3-*O*-rhamnosyl-rhamnosyl-glucoside | -29.04 | -29.49 | -29.18 | 0.230 |
| Chrysoeriol 7-*O*-(6''-malonyl-apiosyl-glucoside) | -28.94 | -29.68 | -29.41 | 0.375 |
| Isorhamnetin 3-*O*-rutinoside | -28.66 | -28.82 | -28.82 | 0.092 |
| Quercetin 3-*O*-xylosyl-rutinoside | -28.23 | -27.80 | -28.42 | 0.318 |
| Myricetin 3-*O*-rutinoside | -28.14 | -28.23 | -28.15 | 0.049 |
| Quercetin 3-*O*-(6''-acetyl-galactoside) 7-*O*-rhamnoside | -28.04 | -27.96 | -28.24 | 0.144 |
| Neodiosmin | -27.33 | -26.13 | -26.15 | 0.687 |
| Kaempferol 3-*O*-(2''-rhamnosyl-galactoside) 7-*O*-rhamnoside | -27.28 | -27.02 | -27.59 | 0.285 |  |
| **Phenolic acids (2 compounds)** |  |  |  |  |
| 1-Sinapoyl-2-feruloylgentiobiose | -28.79 | -28.79 | -28.59 | 0.116 |
| 1,2-Disinapoylgentiobiose | -28.02 | -28.02 | -27.04 | 0.566 |
| **Tannins (8 compounds)** |  |  |  |  |
| Theaflavin 3’-*O*-gallate | -31.77 | -31.92 | -31.22 | 0.369 |
| Procyanidin C1 | -31.27 | -31.59 | -30.37 | 0.633 |
| Theaflavin 3-*O*-gallate | -30.16 | -30.18 | -30.16 | 0.012 |
| Prodelphinidin dimer B3 | -30.14 | -30.39 | -27.26 | 1.739 |
| Epiafzelechin-(4b->8)-epicatechin 3,3’-digallate | -28.89 | -29.65 | -28.61 | 0.538 |
| Procyanidin dimer B2 3’-gallate | -28.10 | -29.07 | -28.28 | 0.516 |
| Procyanidin C2 | -27.01 | -27.18 | -27.45 | 0.222 |
| Procyanidin dimer B5 | -26.94 | -26.89 | -26.59 | 0.189 |

**Table 12S**. Docking results of three simulations on GLP-1 receptor for the top 30 compounds.

|  |  |  |
| --- | --- | --- |
| Compound name | GLP-1 docking score (kcal/mol) | Standard deviation |
| **Simulation 1**  | **Simulation 2** | **Simulation 3** |
| **Anthocyanins (9 compounds)** |  |  |  |  |
| Pinotin A | -14.67 | -12.92 | -12.94 | 1.004 |
| Cyanidin 3-*O*-sophoroside | -13.46 | -12.42 | -12.64 | 0.548 |
| Cyanidin 3-*O*-glucosyl-rutinoside | -13.23 | -13.64 | -13.25 | 0.231 |
| Pelargonidin 3-*O*-sambubioside | -13.55 | -13.65 | -12.74 | 0.499 |
| Malvidin 3,5-*O*-diglucoside | -15.73 | -15.77 | -15.95 | 0.117 |
| Peonidin 3-*O*-rutinoside | -13.31 | -12.66 | -13.46 | 0.425 |
| Pelargonidin 3-*O*-glucoside | -13.26 | -14.12 | -14.21 | 0.524 |
| Cyanidin 3-*O*-xyloside | -14.32 | -14.42 | -14.50 | 0.090 |
| Cyanidin 3-O-galactoside | -14.61 | -14.73 | -14.88 | 0.135 |
| **Flavonoids (12 compounds)** |  |  |  |  |
| Kaempferol 3-*O*-xylosyl-rutinoside | -14.51 | -14.42 | -14.66 | 0.121 |
| Myricetin 3-*O*-rutinoside | -13.16 | -13.33 | -13.44 | 0.141 |
| Quercetin 3-*O*-sophoroside | -13.11 | -13.19 | -12.65 | 0.291 |
| Luteolin 7-*O*-rutinoside | -14.35 | -14.63 | -14.65 | 0.168 |
| Diosmin | -15.80 | -15.91 | -16.03 | 0.115 |
| Hesperidin | -14.18 | -14.09 | -14.30 | 0.105 |
| Kaempferol 3-*O*-xylosyl-glucoside | -13.71 | -13.86 | -13.88 | 0.093 |
| Myricetin 3-*O*-glucoside | -16.24 | -16.35 | -16.46 | 0.110 |
| Apigenin 6,8-C-arabinoside-C-glucoside | -14.49 | -14.43 | -15.15 | 0.400 |
| Quercetin 3-*O*-rutinoside | -13.90 | -14.15 | -14.20 | 0.161 |
| Narirutin | -14.36 | -13.22 | -13.23 | 0.655 |
| Mearnsitrin | -13.41 | -13.38 | -13.22 | 0.102 |
| **Tannins (8 compounds)** |  |  |  |  |
| Theaflavin 3’-*O*-gallate | -13.13 | -13.00 | -13.15 | 0.081 |
| Procyanidin C1 | -15.15 | -15.36 | -15.49 | 0.171 |
| Theaflavin 3-*O*-gallate | -14.16 | -13.13 | -13.87 | 0.531 |
| Prodelphinidin dimer B3 | -14.40 | -13.48 | -14.58 | 0.590 |
| Epiafzelechin-(4b->8)-epicatechin 3,3’-digallate | -13.87 | -14.04 | -13.66 | 0.190 |
| Theaflavin  | -14.49 | -14.46 | -14.55 | 0.046 |
| Castalagin | -14.05 | -13.46 | -13.13 | 0.466 |
| Catechin 3’-glucoside | -13.26 | -13.10 | -13.26 | 0.092 |
| **Tyrosols (1 compound)** |  |  |  |  |
| Demethyloleuropein | -13.81 | -13.50 | -13.58 | 0.161 |